

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form ([see an example](#)) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Yoga respiratory training improves respiratory function and cardiac sympathovagal balance in elderly subjects: randomised controlled trial
AUTHORS	Santaella, Danilo; Silva, António; Rodrigues, Marcos; Amato, Marcelo; Drager, Luciano; Casali, Karina; Montano, Nicola; Lorenzi-Filho, Geraldo

VERSION 1 - REVIEW

REVIEWER	<i>Luciano Bernardi, MD</i> University of Pavia, Italy I declare that I have no competing interest in connection with this paper
REVIEW RETURNED	09-Feb-2011

RESULTS & CONCLUSIONS	<p>This paper describes the effect of a 4-month training program on yoga Pranayama in elderly participants. After the training period, the Authors found an improvement in respiratory and cardiovascular autonomic data in the yoga group, and some minor improvement in the quality of life questionnaire. The paper is very interesting, the study has been well designed and conducted and the results are clearly reported.</p> <p>I have a few minor points that may be helpful for discussion</p> <p>1) I entirely agree that it is vital to calculate the heart rate variability modulation during controlled breathing in this particular subset of patients. In fact, Yoga practitioners tend to breath more slowly and this would have the effect to shift the respiratory sinus arrhythmia into the LF band, thus giving the false impression of increased sympathetic activity, despite an increased parasympathetic predominance. I think that this aspect might be emphasised further in the manuscript.</p> <p>2) On the other hand, when calculating the baroreflex sensitivity, this artifact is eliminated. It was shown in the papers quoted by the authors that slower breathing does improve baroreflex sensitivity and reduces sympathetic activity. Accordingly, Baroreflex sensitivity calculated during spontaneous breathing might have been shown an improvement. If the Authors did collect data also during spontaneous breathing they might want to reanalyse them and verify.</p> <p>3) About the lack of change in baroreflex sensitivity: this can be due to the small sample of participants, as alluded by the Authors, but other possibilities should be considered, in addition to my previous point. In fact, spontaneous baroreflex can be done with several methods, and it was found that these show only fair correlations between them. It is therefore possible that other methods might have shown a different result. The Authors are encouraged to test also additional methods (as those derived from spectral analysis) and</p>
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	perhaps report an average of the different values obtained (see Clin Auton Res. 2010 Dec;20(6):353-61 for more details).
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REVIEWER	<i>Dr JJ van Dixhoorn, MD PhD</i> Centre for Breathing therapy, Amersfoort The Netherlands
REVIEW RETURNED	18-Feb-2011

THE STUDY	Subjects are healthy volunteers, accustomed to yoga practice. The benefit would apply to healthy elderly but frailty with aging is in particular a problem in subjects with health problems, for whom feasibility and effect of practice is not studied.
GENERAL COMMENTS	<p>It is an interesting study that adds to the database of studies that show the effectiveness of tension and breathing regulation for health and disease. My comment regards mainly the issue of generalizability of the findings. The authors state that the outcome indicates a positive shift in outcome of sympathovagal balance, a central modulatory effect and that it may slow down frailty with aging.</p> <p>First, are the techniques really simple as they say. Subjects were volunteers, practicing and attending yoga classes for some (unspecified) time. Yoga bhasrika is a pranayama technique that is usually not taught to beginners, but requires a basic ability to relax, breathe easily and calm the mind. There is no information on the process and success of learning. Did everyone succeed? And, did everyone really practice at home? If not, is there a difference between responders and non-responders? Moreover, What are the chances that subjects continue the practice. We have no information, but in general one may say that a technique has higher chances of being retained in the long term, when it somehow becomes a natural behavior.</p> <p>Second, the outcome measurements are post treatment measures that were taken within a short time frame. There is no certainty whether the measurements taken would hold when taken repeatedly with longer time intervals or during longer time, for instance a 24-hour holter recording of heart rate variability. This was done for instance by Khattab et al, 2007, Complementary & Alternative Medicine, who showed an effect of Iyengar Yoga poses on heart rate variability. Still, a long time follow-up is required to sustain the claim that it may slow down frailty with aging.</p>

VERSION 1 – AUTHOR RESPONSE

We would like to thank the constructive criticism to our work. Dr JJ van Dixhoorn (second reviewer) raised the question regarding how easy it is to learn the exercises. In order to answer the question, we are attaching a film of a subject performing the exercises. We reasoned that the film may be helpful, but we are not sure if the journal format allows such attached files. The subject shown in the film gave us informed consent, and is happy to share his experience. The new version of the manuscript has a sentence (page 12) mentioning the video.

Reviewer: Luciano Bernardi, MD
University of Pavia, Italy

Dear Luciano Bernardi,

The authors would like to thank your work on reviewing our manuscript. In order to facilitate your review process, we have transcribed all your comments, and answered them point by point. We hope our answers meet your expectations.

Sincerely,

Danilo Santaella et al

Reviewer:

This paper describes the effect of a 4-month training program on yoga Pranayama in elderly participants. After the training period, the Authors found an improvement in respiratory and cardiovascular autonomic data in the yoga group, and some minor improvement in the quality of life questionnaire. The paper is very interesting, the study has been well designed and conducted and the results are clearly reported.

Answer:

Thank you for the positive comments.

Reviewer:

I have a few minor points that may be helpful for discussion.

1) I entirely agree that it is vital to calculate the heart rate variability modulation during controlled breathing in this particular subset of patients. In fact, Yoga practitioners tend to breathe more slowly and this would have the effect to shift the respiratory sinus arrhythmia into the LF band, thus giving the false impression of increased sympathetic activity, despite an increased parasympathetic predominance. I think that this aspect might be emphasized further in the manuscript.

Answer:

Thank you for this comment. We have now incorporated this comment in the limitation section, when discussing the aspect of controlled breathing.

2) On the other hand, when calculating the baroreflex sensitivity, this artefact is eliminated. It was shown in the papers quoted by the authors that slower breathing does improve baroreflex sensitivity and reduces sympathetic activity. Accordingly, Baroreflex sensitivity calculated during spontaneous breathing might have been shown an improvement. If the Authors did collect data also during spontaneous breathing they might want to reanalyse them and verify.

Answer:

Unfortunately, we have only collected data during controlled breathing.

3) About the lack of change in baroreflex sensitivity: this can be due to the small sample of participants, as alluded by the Authors, but other possibilities should be considered, in addition to my previous point. In fact, spontaneous baroreflex can be done with several methods, and it was found that these show only fair correlations between them. It is therefore possible that other methods might have shown a different result. The Authors are encouraged to test also additional methods (as those derived from spectral analysis) and perhaps report an average of the different values obtained (see Clin Auton Res. 2010 Dec;20(6):353-61 for more details).

Answer:

We have tested the BRS alpha, one of the methods suggested by the reviewer that derived from spectral analysis. We have calculated spontaneous baroreflex in the low frequency (BRS-LF) and high frequency (BRS-HF) as the squared root of the ratio of the autoregressive powers of RR interval

and SBP series in the low, and high frequency ranges, respectively. The results are presented below, and also show no differences between groups. For the sake of simplicity, we did not add all this new analysis to the paper. The results are presented below.

Control Yoga

Variables Baseline 4 Months p Value Baseline 4 Months p Value

Alpha LF 8.26 ± 10.48 5.44 ± 3.33 0.30 13.12 ± 14.30 9.03 ± 8.03 0.38

Alpha HF 7.38 ± 5.05 8.10 ± 4.96 0.71 9.06 ± 6.73 7.87 ± 5.70 0.63

Reviewer: Dr JJ van Dixhoorn, MD PhD
director
Centre for Breathing therapy, Amersfoort
The Netherlands

Dear Dr. JJ Van Dixhoorn,

The authors would like to thank your work on reviewing our manuscript. In order to facilitate your review process, we have transcribed all your comments, and answered them point by point. We hope our answers meet your expectations.

Sincerely,

Danilo Santaella et al

Reviewer:

Subjects are healthy volunteers, accustomed to yoga practice. The benefit would apply to healthy elderly but frailty with aging is in particular a problem in subjects with health problems, for whom feasibility and effect of practice is not studied.

Answer:

We agree with the reviewer. This limitation was added to the manuscript.

Reviewer:

It is an interesting study that adds to the database of studies that show the effectiveness of tension and breathing regulation for health and disease.

Answer:

Thank you for the positive comment.

Reviewer:

My comment regards mainly the issue of generalizability of the findings. The authors state that the outcome indicates a positive shift in outcome of sympathovagal balance, a central modulatory effect and that it may slow down frailty with aging.

First, are the techniques really simple as they say? Subjects were volunteers, practicing and attending yoga classes for some (unspecified) time. Yoga bhasrika is a pranayama technique that is usually not taught to beginners, but requires a basic ability to relax, breathe easily and calm the mind. There is no information on the process and success of learning. Did everyone succeed? And, did everyone really practice at home? If not, is there a difference between responders and non-responders? Moreover, what are the chances that subjects continue the practice. We have no information, but in general one

may say that a technique has higher chances of being retained in the long term, when it somehow becomes a natural behaviour.

Answer: The respiratory exercises are relatively simple (see video attached). However, this technique is not taught to beginners. This limitation was clearly stated in the new version of the manuscript. In our study we recruited highly motivated practitioners that complied to the protocol (absence of compliance was actually a exclusion criterion). We therefore have no data to compare responders and non-responders. We made this point clear in the limitation section.

Concerning the chances of the practice being retained in the long term, some subjects, who are still enrolled in the course, have declared spontaneously that they have being practicing it in a regular basis. However, further studies are necessary to determine the long term compliance.

Reviewer:

Second, the outcome measurements are post treatment measures that were taken within a short time frame. There is no certainty whether the measurements taken would hold when taken repeatedly with longer time intervals or during longer time, for instance a 24-hour holter recording of heart rate variability. This was done for instance by Khattab et al, 2007, Complementary& Alternative Medicine, who showed an effect of Iyengar Yoga poses on heart rate variability. Still, a long time follow-up is required to sustain the claim that it may slow down frailty with aging.

Answer:

The reviewer is correct. We have not data to show the effects of our exercises over longer periods of time with methods such as 24-hour holter recording. However, the data acquisition was performed in the morning period, and all subjects were instructed not to perform the exercises in the morning of data acquisition. Therefore, the last practice was performed in the previous evening (~ 16 hrs before data acquisition). Because the concept is to practice Bhastrika pranayama twice a day, we have indirect evidence that the beneficial effects are sustained over the 24-h period.

We agree with the reviewer that we have no data to claim that the exercises may slow down the frailty with aging. We made clear in the new version of the manuscript that this statement is a speculation that will need to be further investigated.

VERSION 2 - REVIEW

REVIEWER	<i>Dr JJ van Dixhoorn</i>
REVIEW RETURNED	31-Mar-2011

GENERAL COMMENTS	Please continue the good work. It will be very interesting to see the effects on elderly subjects with frailty or comorbidity and to assess how well they will be able to perform the exercises. My guess is that when they do perform, the effects will be substantial.
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